P2-052 BSTB: Molecular Targets Posters, Tue, Sept 4

Effects of huTNF-α, hIL-2 gene transfection on the expressionof MDR1, LRP gene in lung cancer

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Background: To study the effects of huTNF-#&03b1; and hIL2 gene transfection on the expression of MDR1 and LRP genes in lung cancer cell lines.

Methods: huTNF-#&03b1; and hIL2 gene plasmids were constructed and transfected into A549, GLC-282, H446 and H460 cells with lipofectinmin. Positive clones were screened out by G418. The expressions of MDR1 and LRP genes were detected at mRNA level by reverse transcription polymerase chain reaction (RT-PCR) in the non2transfected cells and the cloned cells.

Results: MDR1 gene was positive in A549, GLC-82, H446 and H460 cell lines, LRP gene was positive in A549, GLC-282 and H460 cell lines; The transfected cell lines expressed both huTNF-#&03b1; and hIL2 gene, and the A549, H446 and H460 cell lines transfected with hIL2 gene had no MDR1 expression at mRNA level compared with the non2transfected ones.

Conclusion: MDR1 and LRP genes are expressed in lung cancer cell lines, which indicates the presence of intrinsic drug resistance before any form of therapy. MDR1 gene is not expressed in hIL2 transfected cell lines, which demonstrates that hIL2 gene modulates the MDR1 gene expression at mRNA level, and may reverse the multidrug resistance of lung cancer.

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Establishment, identification and examination about the EGFR status of the lung cancer cell line

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Objective: To establish and identify a lung cancer cell line by primary culture and examine the EGFR status of the cell line.

Methods: The tumor cell was isolated from the tumor specimen by enzyme digestion and cultured in RPMI-1640. The cell line which had been cultured for over 60 passages was identified with cell grow curve, chromosome analysis, cell cycle by Flow Cytometry, soft agar colony forming test and tumorgenesis test in mice. After PCR amplification of the 18, 19, 21 exon of EGFR gene and purification of the PCR products, EGFR mutation of the exons was sequenced by using ABI 3100. EGFR gene copy number was measured by Fluorescent In Situ Hybridization (FISH).

Results: One cell line was obtained from tumor specimen by enzyme digestion and had been cultured for more than 60 passages. The grow curve show that the doubling time of the cell line was 27.1 hours. The number of chromosome is 66-78 and the chromosome was triploid showing abnormal karyotypes. Cell cycle detected by Flow Cytometry show that there are 69.05% cells within G1 stage, 11.32% cells within G2 stage and 19.63% cells within S stage. The soft agar colony forming rate was 27.3% and the cell line exhibit great tumorigenesis activity in athymic mice. The sequences of exon 18, 19, 21 show that EGFR gene of the cell line was wild type and the gene copy number of the cell line detected by FISH was balanced polysomy.

Conclusions: The cell line from is identified to be the EGFR gene wild type and high copy number. EGFR mutation is not correspondence to the EGFR copy number. The patients with EGFR gene wild type and high copy number may have good response to EGFR-TKI.

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Combination treatment with arsenic trioxide and sulindac induces apoptosis of NCI-H157 human lung carcinoma cells via activation of mitogen-activated protein kinases

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The arsenic trioxide (As203) has been introduced to the treatment of acute promyelocytic leukemia, and induced apoptosis in a variety of solid tumor cell lines. Non-steroidal anti-inflammatory drugs (NSAIDs) are known to enhance the responsiveness of tumor cells toward chemotherapeutic drugs. We previously demonstrated that combination treatment with arsenic trioxide and sulindac augments their apoptotic potential in lung cancer cells through activation of caspase cascade and mitochondrial dysfunction. However, the previous mechanism of synergistic enhancement in tumoricidal activity is not clearly known yet. Herein, we demonstrated that combination treatment of As203 and sulindac resulted in a synergistic augmentation of cytotoxicity and induced apoptosis in NCI-H157 lung cancer cells. Moreover the combination increased ROS levels compared with individual treatment. In addition, it further strongly induced HO-1 expression, activated stress-activated mitogen-activated protein kinases (MAPK), and DNA damage. Inhibition of either JNK or p38 kinase partially inhibited the augmented cell death and attenuated apoptosis by combination treatment. In conclusion, the results showed that synergistic augmentation of cytotoxicity was partially involved by MAPK signaling pathway.

BSTB: Others

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A serum proteomic analysis of lung squamous cell carcinoma.

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Background: Lung cancer accounts for the death of approximately 160,000 Americans annually and is the most common cause of cancer mortality in developed nations. Comprising more than 30% of all cancer deaths in the U.S., mortality from lung cancer exceeds the estimated values for cancer of the breast, prostate, colon and rectum combined. Non-small cell lung cancer (NSCLC) is a heterogeneous collection of histological sub-types that accounts for approximately 80% of all lung cancer in the United States. The primary objective of this project is to identify new biomarkers for early squamous cell carcinoma (SCC)